

OCT 09 2003

AMENDMENTS TO THE SPECIFICATION

TECH CENTER 1600/2900

1. Please amend the paragraph beginning on page 1, line 26 and ending on page 2, line 4, as follows:

The present invention is directed to a method of screening test compounds for probable biological properties based principally on correlation of numerical values characteristic of their interaction with two or more membrane mimetic surfaces with corresponding values for control compounds of known biological activities/function. The method is grounded on the premise that compounds with similar sets of membrane binding properties will have similar pharmacological properties and/or biological activities. The membrane binding properties of test compounds can be calculated, or they can be determined empirically with use of, for example, liposomes, immobilized artificial membranes, such as those described in U.S. Patent 4,931,498, the disclosure of which is incorporated herein by reference, ~~Langmuir-Blodgett~~ Langmuir-Blodgett films, computer chips or similar devices with immobilized lipids, capillary zone electrophoresis columns coated with membrane lipids, and the like.

2. Please amend the paragraph beginning on page 16, line 8 and ending on page 17, line 12, as follows:

That phenomenon (the grouping of membrane mimetic binding data as vectors in "membrane space") forms the basis of the present invention and allows multiple membrane binding constants to serve as a predictor of biological activity. While Figs. 1 and 2 are illustrated as the products of pattern matching by vector analysis, other art-recognized mathematical analytical techniques such as multivariate analysis and principal component analysis can be applied to membrane binding data to compare test compounds with control compounds with known biological function. Vector analysis is particularly useful for pattern matching in accordance with this invention in that it can be carried out, albeit not graphically represented, in more than three dimensions. Such techniques can also be applied to data sets that include, in addition to data characteristic of multiple membrane mimetic surfaces,

such as data characteristic of reversed-phase chromatography, supports in high performance liquid chromatography system, other techniques can be used, for example, computer chips or similar devices with immobilized lipids, capillary zone electrophoresis

columns coated with membrane lipids, ~~Langmuir-Blodgett~~ Langmuir-Blodgett films, liposomes, and adsorbed monolayers of lipids on any surface, for example an AFM tip and evaluating the change in oscillation of the tip in the presence of test and control compounds. In addition to such empirical data acquisition techniques, numerical values characteristic of both MAF and non-MAF parameters can be obtained by computer calculations. Thus data sets for use in accordance with this invention can include calculated non-MAF parameters, and calculated MAF parameters including simulated MAF properties. "Calculated non-MAF parameters" as used in describing the present invention are numerical quantities that can be derived from a known chemical structure. Examples include surface area, polar surface area, number of H-bonds, topological indices, solubility, etc. These parameters alone do not predict the general membrane binding properties, *i.e.*, MAFs, of compounds. The term "calculated MAF parameters" refers to a combination of calculated non-MAF parameters, with or without individual membrane binding constants, that can be used to predict Membrane Affinity Fingerprints (MAF). Since HPLC retention times can be used to calculate membrane binding constants, methods used to calculate retention times of solutes are actually calculating MAF parameters. An example of a calculated retention time for 12 compounds can be found in (Amie, D. Davidovic-Amie, D. Trinajstić, N., *J. Chem. Inf. Comput.* 1995, 35, 136-139.) The term "simulated MAF" refers to a calculated MAF parameter obtained from Molecular Dynamics Simulations of compounds with IAMs, bilayer membranes, other membrane mimetic surfaces, or a force field characteristic of these membranes.